

IN THE SPECIFICATION

A marked-up version of the following amended paragraphs is attached hereto as Exhibit C. Additions are shown by underlining and deletions are shown by brackets.

Please amend the specification as follows:

On page 8, please replace the paragraph beginning, "Figure 13:" with the following paragraph:

--Figure 13: The amino acid sequence of rat Nogo A (SEQ ID NO:2) aligned with the theoretical amino acid sequence of human Nogo (SEQ ID NO:29). The human Nogo amino acid sequence was derived from aligning expressed sequence tags (EST) to the rat Nogo sequence and translating the aligned human ESTs using the rat Nogo as a guiding template.--

On page 15, please replace the paragraph beginning, "Moreover, the present invention..." with the following paragraph:

--Moreover, the present invention provides and includes the predicted amino acid sequence of the human Nogo protein, and fragments thereof. As shown in Figure 13, the amino acid sequence of rat Nogo protein (Figure 2a; SEQ ID NO:2) is aligned with the predicted amino acid sequence of human Nogo protein (Figure 13; SEQ ID NO:29). Accordingly, the present invention encompasses human Nogo proteins comprising the predicted amino acid sequence of human Nogo, Figure 13 and SEQ ID NO:29, or a subsequence of the predicted amino acid sequence of human Nogo, consisting of at least 6 amino acid residues, or one or more of the following predicted amino acid sequences of human Nogo fragments: MEDLDQSPLVSSS (Human Nogo, corresponding to amino acids 1-13 with SEQ ID NO:43), KIMDLKEQPGNTISAG (Human Nogo, corresponding to amino acids 187-203 with SEQ ID NO:44), KEDEVVSSEKAKDSFNEKR (Human Nogo, corresponding to amino acids 340-358 with SEQ ID NO:45), QESLYPAAQLCPSFEESEATPSPVLPDIVMEAPLNSAVPSAGASVIQPSS (Human Nogo, corresponding to amino acids 570-619 with SEQ ID NO:46). Naturally occurring human Nogo and recombinant human Nogo, and fragments thereof having an amino acid sequence

substantially similar to the above-described amino acid sequences and able to be bound by an antibody directed against a Nogo protein are within the scope of the invention.--

AC On page 15, please replace the paragraph beginning, "The present invention further provides" with the following paragraph:

--The present invention further provides nucleic acid molecules that encodes a human Nogo protein having an amino acid sequence substantially similar to the amino acid sequence as shown in Figure 13 (Figure 13; SEQ ID NO:29). In specific embodiments, nucleic acid molecules encoding fragments of human Nogo protein having an amino acid sequence substantially similar to the amino acid sequence as shown in Figure 13 (SEQ ID NO:29) are also contemplated with the proviso that such nucleic acid molecules do not comprise the nucleotide sequence of the above-identified human ESTs.--

AC Please replace the paragraph spanning pages 17 and 18 and beginning with "To perform functional analysis of various regions" with the following paragraph:

--To perform functional analysis of various regions of Nogo, a series of deletions in the *Nogo* gene has been generated and cloned into an expression vector by recombinant DNA techniques and expressed as a fusion protein. Nucleic acids that encode a fragment of a Nogo protein are provided, e.g., nucleic acids that encode amino acid residues 1-171, 172-974, 259-542, 542-722, 172-259, 722-974, or 975-1162 of SEQ ID NO: 2, or combinations thereof; and nucleic acids that encode amino acid residues 1-131, 132-939, 206-501, 501-680, 132-206, 680-939, and 940-1127 of SEQ ID NO:29, or combinations thereof. Some of the deletion constructs comprises truncated portions of Nogo and additional nucleotide sequences encoding a hexahistidine tag and/or a T7-tag. Nucleic acids encoding truncated Nogo proteins that lacks amino acid residues 172-259, amino acid residues 974-1162, or amino acid residues 172-259 and 974-1162, of SEQ ID NO:2 but otherwise comprises the remainder of SEQ ID NO: 2; or amino acid residues 132-206, amino acid residues 939-1127, or amino acid residues 132-206 and 939-1127, of SEQ ID NO:29 but otherwise comprises the remainder of SEQ ID NO:29, are provided. The structure of exemplary deletion constructs are shown in Figure 18. The deletion constructs produce fragments or truncated portion(s) of Nogo when

introduced into a cell. The biological activities of these mutants were tested in various functional assays as described in Table 2 in Section 6.2.7.--

On page 22, please replace the paragraph beginning with "Nucleotide sequences encoding fragments" with the following paragraph:

--Nucleotide sequences encoding fragments of human Nogo A comprising an amino acid sequence selected from the group consisting of amino acid residues 1-131, 132-939, 206-501, 501-680, 132-206, 680-939, and 940-1127 of SEQ ID NO:29 are also provided. Nucleotide sequences that encodes truncated portions of human Nogo A are also provided; the truncated proteins lack amino acid residues 132-206, amino acid residues 939-1127, or amino acid residues 132-206 and 939-1127, of SEQ ID NO:29 but otherwise comprises the remainder of SEQ ID NO:29.--

On page 26, please replace the paragraph beginning with "In a specific embodiment of the present invention" with the following paragraph:

--In a specific embodiment of the present invention, such Nogo proteins, whether produced by recombinant DNA techniques or by chemical synthetic methods or by purification of native proteins, include but are not limited to those containing, as a primary amino acid sequence, all or part of the amino acid sequence substantially as depicted in Figure 2a (SEQ ID NO:2), bovine in Figure 12 (SEQ ID NO:28), or human in Figure 13 (SEQ ID NO:29), as well as fragments and other derivatives (such as but not limited to those depicted in Figure 18), and analogs thereof, including proteins homologous thereto. Preferably, the Nogo proteins of the invention are free of all CNS myelin material with which it is normally associated.--

On page 28, please replace the paragraph beginning with "Various procedures known in the art" with the following paragraph:

--Various procedures known in the art may be used for the production of polyclonal antibodies to a Nogo protein or derivative or analog. In a particular embodiment, rabbit polyclonal antibodies to an epitope of a Nogo protein encoded by a sequence of SEQ ID NO:2 in Figure 2a, SEQ ID NO:28 in Figure 12, SEQ ID NO:32 in Figure 14, or SEQ ID

NO:29 in Figure 13, (rat Nogo A, bovine Nogo, rat Nogo C, or human Nogo respectively) or a subsequence thereof, can be obtained. For the production of antibody, various host animals can be immunized by injection with the native Nogo protein, or a synthetic version, or derivative (e.g., fragment) thereof, including but not limited to rabbits, mice, rats, etc. Various adjuvants may be used to increase the immunological response, depending on the host species, and including but not limited to Freund's (complete and incomplete), mineral gels such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanins, dinitrophenol, and potentially useful human adjuvants such as BCG (bacille Calmette-Guerin) and *corynebacterium parvum*.--

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On page 30, please replace the paragraph beginning with "In order to map the active region(s) of Nogo" with the following paragraph:

In order to map the active region(s) of Nogo, a series of Nogo deletion mutants have been prepared by recombinant DNA techniques as described in Section 6.2.7. The portions of Nogo which are present in the deletion mutants are shown in Figure 18. In a specific embodiment, the invention provides fragments of Nogo e.g., fragments comprising (or alternatively consisting of) Nogo A (SEQ ID NO: 2) amino acid numbers 1-171, 172-974, 259-542, 542-722, 722-974, 172-259, or 975-1162, or combinations of the foregoing.

Truncated mutants of Nogo lacking amino acid numbers 172-259 and/or 975-1162 of SEQ ID NO:2 are also provided, as these regions appear to be non-essential and can be removed from Nogo without affecting biological activity. The corresponding fragments of human Nogo A comprising (or alternatively consisting of) amino acid numbers 1-131, 132-939, 206-501, 501-680, 132-206, 680-939, or 940-1127 of SEQ ID NO:29 are also provided. Truncated mutants of human Nogo A are also provided which lack amino acid numbers 132-206, amino acid residues 939-1127, or amino acid residues 132-206 and 939-1127, of SEQ ID NO:29.

AB
On page 69, please replace the paragraph beginning with "The instant invention provides" with the following paragraph:

--The instant invention provides the nucleotide sequences encoding human Nogo protein, and fragments of human Nogo proteins, including the human equivalents to rat Nogo